gene, wherein the expression of said *bax* gene would sensitize said tumor cells.

REMARKS

Amendment

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

The 35 U.S.C. §112 Rejection

Claims 2-3 and 5-10 were rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The rejection is respectfully traversed.

The present invention is drawn to the induction of apoptosis and inhibition of cell growth by inducible expression of the Bax gene. Expression of Bax resulted in apoptotic cell death in human ovarian cancer cells but not in normal human peritoneal mesothelial cells (Examples 6-8, 30 and 31). Bax expression also sensitized refractory cancer cells to radiation (Examples 9, 20 and 21). It was further shown that overexpression of Bax significantly enhanced

chemotherapy-induced cytotoxicity in both established cell lines and primary tumor cells (Example 32). These data showed that overexpression of Bax alone or in combination with radiation or chemotherapy is useful in inhibition of tumor cell growth.

Applicants hereby submit data that shows the effects of Bax overexpression can be generalized to other types of tumor cells. As shown in the attached Declaration of the co-inventor, Dr. David Curiel, a synergistic radiosensitizing effect of Bax can be induced in refractory glioblastoma cell after gene delivery via recombinant adenovirus. This result was confirmed in an *in vivo* murine xenograft model of glioblastoma. Toxicity was selectively induced in tumors but normal astrocytes were spared, thereby demonstrating the clinical utility of combining *bax* gene delivery with radiotherapy for the treatment of malignant brain tumors.

Based on a fair reading of the data contained herein, Applicants submit that the methods claimed herein have reasonable correlation to the scope of the enablement provided. Accordingly, Applicants respectfully request that the rejection of claims 2-3 and 5-10 under 35 U.S.C. §112, first paragraph, be withdrawn.

The 35 U.S.C. §103(a) Rejection

Claims 1-2 was rejected under 35 U.S.C. §103(a) as being unpatentable over **Seth** et al. in view of **Sato** et al. and **Anton** et al. The rejection is moot because claims 1 and 2 have been cancelled.

This is intended to be a complete response to the Final Office Action mailed August 28, 2002. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: Feb 3, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 3 has been amended as follows:

3. (twice amended) A method of treating an individual having a neoplastic disease, comprising the step of administering to said individual a ~~an a mount of the~~ composition comprising an inducible recombinant adenoviral vector encoding a pro-apoptotic *bax* gene which is placed downstream of a loxP excision cassette and a vector encoding a protein that induces the expression of said *bax* gene, wherein the expression of said *bax* gene would induce apoptosis and inhibit tumor cell growth. ~~of claim 2 effective to inhibit neoplastic growth.~~

Claim 7 has been amended as follows:

7. (twice amended) A method of treating an individual having ovarian cancer, comprising the step of administering to said individual a composition comprising an inducible recombinant adenoviral vector encoding a pro-apoptotic *bax* gene which is placed downstream of a loxP excision cassette and a vector encoding a protein that induces the expression of said *bax* gene, wherein the